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IRITIS AND OTHER OCULAR LESIONS ON INTRAVENOUS INJECTION OF STREPTOCOCCI *

WITH PLATES 6-8

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In a previous paper[1] I pointed out that streptococci from rheumatic arthritis and myositis, when injected intravenously into animals, are prone to lodge in the capillaries of the iris, producing iritis and other lesions of the eye. Now, I wish to record further observations with illustrative experiments the results of which indicate that iritis and certain other lesions of the eye, generally thought to be toxic, may be infectious in nature.

As the outcome of a long series of experiments in which animals were injected intravenously under uniform conditions with streptococci from rheumatism, from appendicitis, from ulcer of the stomach, from cholecystitis, from erythema nodosum, from herpes zoster, from parotitis, from pyorrhea, from tonsils, and from dairy products, I have had opportunity to study the eye lesions in forty-eight animals. The lesions may be classified as follows: (1) unilateral panophthalmia in five instances (twice following injections of strains from rheumatism and herpes zoster as isolated, and once in each case after one animal passage, and once in a rabbit injected with a streptococcus mucosus from the eyeball in a case (for which I am indebted to Dr. Lane) of metastatic panophthalmia following tonsillitis and otitis media); (2) hemorrhages in the limbus, with or without episcleritis, in fourteen instances (four times following injection of laboratory strains after they had attained a certain grade of virulence, three times with rheumatic strains, twice with strains from appendicitis, twice with strains from herpes zoster, and once each with strains from erythema nodosum, myositis, and from butter); (3) iritis or iridocyclitis nine times (four times after injection of certain laboratory strains, three times with rheumatic strains, and twice following injection of streptococci from small pus pockets in tonsils of otherwise normal individuals); (4)

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[1] Jour. Infect. Dis., 1914, 14, p. 61.

conjunctivitis, usually bilateral, occurring frequently, in ten instances associated with the streptococci injected (once each with streptococci from appendicitis, herpes zoster, and rheumatism, once with streptococci from butter, once with streptococci from the pus pocket in the tonsil of a cow, twice after injection of a laboratory strain, and three times after injection of strains from pus pockets in tonsils from approximately 100 individuals); (5) ulcer of the cornea due to the organism injected, observed only once, after injection of a strain of streptococcus from the muscle in calcifying myositis in a man. Lesions similar to these occurred with or without herpes in twelve animals injected with the strains from herpes zoster. Herpes of the conjunctiva followed injections of streptococcus from the tonsil in ulcer of the stomach in a cow. Hemorrhages in the retina were not often looked for, but were found in two instances.

It must not be supposed that the occurrence of these lesions is accidental because they appear to occur commonly only after injections of strains as isolated in rheumatic arthritis and myositis (17 percent) and in herpes zoster (15 percent), while after injections of strains from appendicitis, ulcer of the stomach, cholecystitis, and erythema nodosum, eye lesions are extremely rare. Moreover, strains from various sources may be made to acquire affinity for the eye. Thus, Strain R 51 A, which had been isolated eleven years previously as a pneumococcus and which had long since lost its virulence, was passed successively through eighteen animals without producing eye lesions in a single instance; but, in the eighteenth passage, it produced suppurative conjunctivitis in the only rabbit injected. In the nineteenth passage, it produced iritis (rabbit). In the twentieth passage, it produced suppurative conjunctivitis associated with iritis and marked hemorrhages and infiltration at the limbus in a dog, and marked conjunctival and scleral hemorrhages, especially at the limbus, in a rabbit. Subsequent passages failed to produce eye lesions. Exactly similar results were obtained from injection in successive animals of two strains of pneumococci, which at the time grew as streptococci, and which had lost their virulence by long cultivation on artificial media; each produced iritis in the tenth and fourteenth animal passage, while all the other injections failed to produce eye lesions. The injection of Strain 12, which originally had been isolated as a hemolytic streptococcus from "milk slime," but which had lost its hemolytic property and had acquired the properties of a typical streptococcus viridans by growth in symbiosis with Bacillus subtilis on blood agar plate, produced no eye lesions in the first seven injections, but in the eighth animal passage produced hemorrhages about the limbus and several in the retina in two rabbits injected, while in all subsequent passages no eye lesions developed. Finally, if the lesions in the eye really depend on a certain quality or virulence of the streptococci, then the associated lesions in the other organs should be similar, following injection of the different strains, at the time the eye lesions develop. This, on analysis, is found actually to be the case. Thus, of forty-eight animals showing eye lesions, twenty-eight showed arthritis, usually mild; five showed hemorrhages in the appendix; eight, ulcer of the stomach; ten, lesions of the endocardium; eight, of the pericardium; nineteen, of the muscles or fascia; and twelve, of the kidneys. The incidence and character of associated lesions in animals, therefore, correspond closely to what is observed in man. It must not be supposed, however, that the occurrence of eye lesions at a certain grade of virulence holds only for streptococci. Similar results have been obtained from injection of colon bacilli and staphylococci.

The lesions were usually acute and consisted of extravasation of red blood corpuscles and a variable infiltration of leukocytes. Suppurative iritis was observed only once (see Fig. 1). In the instances of panophthalmia, there was turbidity of the aqueous humor, which contained leukocytes and from which the organisms injected could usually be isolated in pure culture.

The organism injected was demonstrated in the lesions in large or small numbers by cultural methods and in sections in a large number of instances, sometimes after the animals had recovered and the blood was sterile. In fact, so constantly was the organism injected found that one feels almost justified in concluding that the occurrence of a localized hemorrhage, for instance, means the presence in it of bacteria. This holds true, not only in the case of streptococci, but in that of staphylococci and colon bacilli as well.

The bacteria were found within blood vessels adjoining the lesions and in the areas of hemorrhage and infiltration, usually with aggregation of leukocytes and endothelial cells. At times, when the animal survived the injection, active phagocytosis by leukocytes and endothelial cells could be made out. Smears from the pus in the conjunctival sac in instances of conjunctivitis which were observed in rabbits, dogs, and one monkey, and in the instances of panophthalmia, commonly showed diplococci within and without leukocytes. Plate cultures on blood agar and fermentative tests were used to establish the identity of the organisms injected and of those found in the inflamed conjunctival sac. The cultures, made after repeated washing of the muco-purulent material in salt solution, at times yielded the organism injected in pure culture; usually, however, together with a variable number of other bacteria, mostly saprophytic bacilli Not all instances of conjunctivitis were due to the streptococci injected. The frequent occurrence of lesions about the ciliary body or the iris and the limbus needs special emphasis. This might be thought to be due to the fact that here, as in the structure about the joints and the more tendinous portion of muscles, there is a gradation from an abundant to a very scanty blood supply, and hence a gradation of the supply of available oxygen, thus inviting localization and affording opportunity for the growth of bacteria, a circumstance which for the same reasons would make for lesions by circulating toxic substances, no matter from what source.

The following experiments will serve to illustrate the results obtained:

RABBIT 581.—Large, black rabbit, injected intravenously, Dec. 31, 1913, with the growth from 45 c.c. of ascites dextrose broth of Streptococcus 839, which had been isolated from under the crust of a crushing injury of the thumb in a case of acute rheumatic fever with pericarditis in a young man 19 years old.

Jan. 3, 1914.—The rabbit died at 12 noon. Examined at once: Marked circumcorneal congestion of the left eye; fluid in the anterior chamber distinctly turbid; anterior portion of the iris covered with a plastic, slightly adherent exudate, smears of which showed leukocytes and numerous diplococci; the lens and other structures of the eye apparently normal; the right eye normal; the joint and pericardiac fluids distinctly turbid and increased in amount; a number of whitish areas associated with hyperemia and hemorrhage in the muscles, especially in the subscapular muscles of the right side and in the muscles of the spine; one rather large hemorrhage in the mucous membrane of the pylorus of the stomach; spleen distinctly enlarged, and hyperemic; no other gross lesions.

Jan. 4, 1914.—Cultures from the blood showed a few streptococci; cultures from the pericardiac and joint fluids gave a moderate number, while cultures from the fluid in the anterior chamber of the left eye gave an enormous number of colonies of streptococci only, which produced a slight hazy zone of hemolysis on blood agar plates; cultures of the fluid in the anterior chamber of the right eye, sterile. Sections of the eye showed marked necrosis and leukocytic infiltration of the iris, most marked over the anterior layer where there were very many diplococci (see Figs. 1 and 2).

RABBIT 61.—Medium-sized Belgian hare, injected intravenously, March 4, 1914, with the growth from 45 c.c. of ascites dextrose broth of a streptococcus isolated from a small quantity of pus expressed from the tonsil ten days after an attack of recurring herpes involving the thigh.

March 6.—Seemed ill. Chloroformed and examined at once: Two sharply circumscribed areas of hemorrhage and edema of the right eye, one (0.3 cm.) directly opposite the attachment of the iris near the limbus, the other (0.5 cm.)

situated just where the external rectus merges into the sclera (Fig. 3); the blood vessels surrounding these areas showed congestion; the iris showed no visible changes; the fluid in the anterior chamber clear; moderate increase in amount and turbidity of the joint fluid in both knees and wrist joints; intussusception of ileum associated with plastic adhesions; no other focal lesions.

March 8.—Cultures made from the blood, joint fluids, and fluid in the anterior chamber of the right eye were sterile. Sections of the eye showed subscleral hemorrhages associated with beginning round cell infiltration just outside of the attachment of the iris in the ciliary body. A thorough search for bacteria in gram-stained sections showed a few diplococci, free and within leukocytes and endothelial cells, one of which is shown in Fig. 4.

RABBIT 70.—Medium-sized, white rabbit, injected intravenously, March 4, 1915, with the growth from 15 c.c. of ascites dextrose tissue broth of a streptococcus mucosus in the second culture, isolated from the eyeball during recovery from metastatic panophthalmia in a middle-aged man.

March 6.—Seemed well; marked lacrimation and circumcorneal injection of blood vessels of the left eye; the cornea opaque, and the fluid in the anterior chamber turbid. Chloroformed: A whitish-gray, radiating deposit on the anterior surface of the iris, smears from which showed many leukocytes and other cells and a moderate number of diplococci with a distinct capsule; no other lesions; sections of the iris and adjacent structures showed hyperemia and moderate leukocytic infiltration, but unfortunately the film of exudate was largely lost in the preparation. However, a search for bacteria showed a number of diplococci near the attachment of the iris and a short chain of diplococci in the anterior chamber just outside an area of hemorrhage in the iris (Fig. 5).

RABBIT 945.—Small, white rabbit, injected intravenously, Nov. 23, 1914, with the growth from 15 c.c. of dextrose broth of a colon bacillus isolated from the wall of the appendix in a case of subacute appendicitis.

Nov. 24.—Found dead: Numerous hemorrhages in the conjunctiva and in the limbus of right eye (Fig. 6); marked subperitoneal and mucous hemorrhages throughout the appendix; moderate hemorrhages in Peyer's patches and mucous membrane of the duodenum, colon, and sigmoid and in common and hepatic ducts and apex of the gall-bladder; a few punctate hemorrhages in the myocardium and skeletal muscles.

Nov. 25.—Cultures from blood and areas of hemorrhage showed large numbers of colon bacilli. Sections of the hemorrhagic area in the eye showed a large number of bacilli with varying degrees of decolorization when stained by Gram's method (Fig. 7).

EXPLANATION OF PLATES 6-8

Fig. 1.—Section of iris and ciliary body of rabbit showing marked leukocytic infiltration four days after an intravenous injection of streptococcus from rheumatic arthritis. Hematoxylin and eosin. × 60.

Fig. 2.—Streptococci in area of infiltration in Figure 1. Gram-Weigert stain. × 1200.

Fig. 3.—Localized hemorrhages in the sclera near the limbus and at the attachment of the external rectus muscle in rabbit forty-eight hours after an intravenous injection of streptococcus from pus pocket in tonsil. × 3½.

Fig. 4.—Diplococcus adjacent to area of hemorrhage in Figure 3. × 1200.

Fig. 5.—Diplococci in anterior surface of iris just opposite an area of hemorrhage into the iris. See Rabbit 70. Gram-Weigert stain. × 1200.

Fig. 6.—Section of limbus of eye in rabbit showing hemorrhage and slight leukocytic infiltration twenty-four hours after intravenous injection of colon bacilli. Hematoxylin and eosin. × 430.

Fig. 7.—Colon bacilli in varying stages of decolorization in area of hemorrhage shown in Figure 6. ×.1200.

PLATE 6

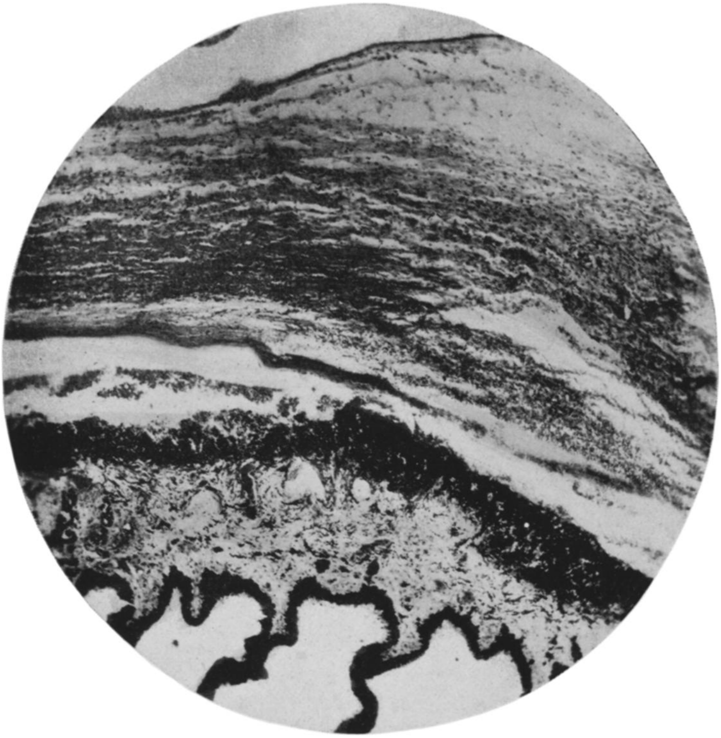

Figure 1.

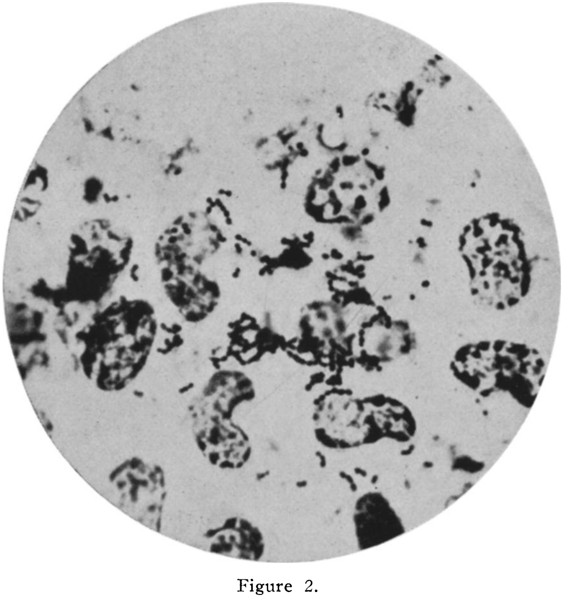

Figure 2.

Plate 7

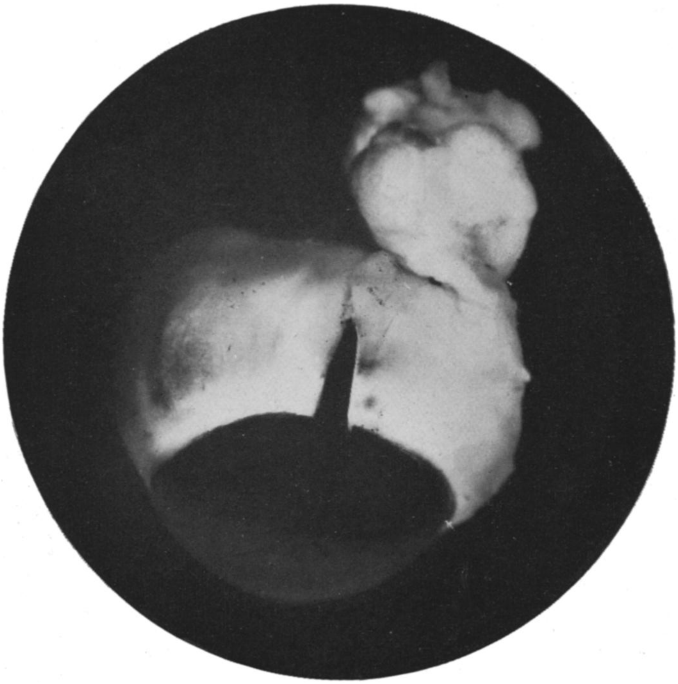

Figure 3.

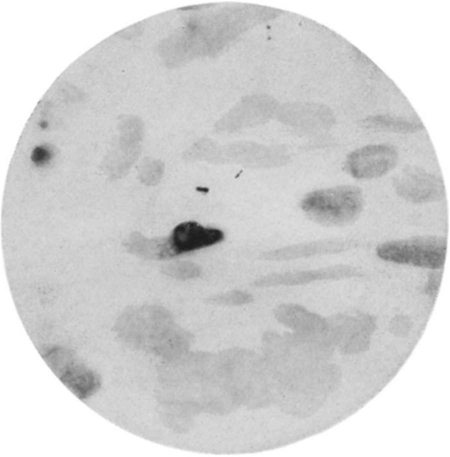

Figure 4.

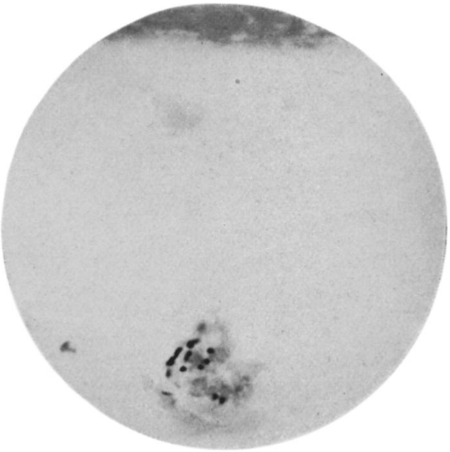

Figure 5.

PLATE 8

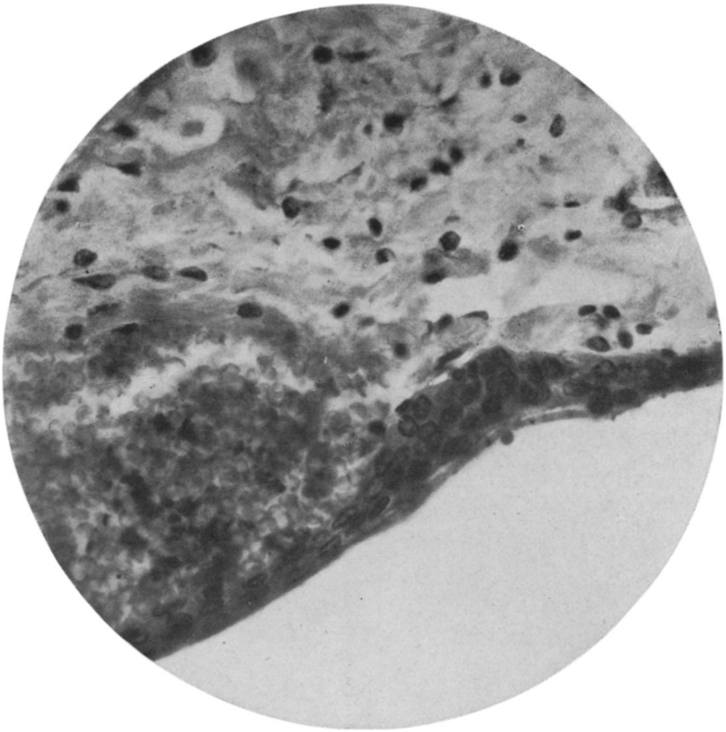

Figure 6.

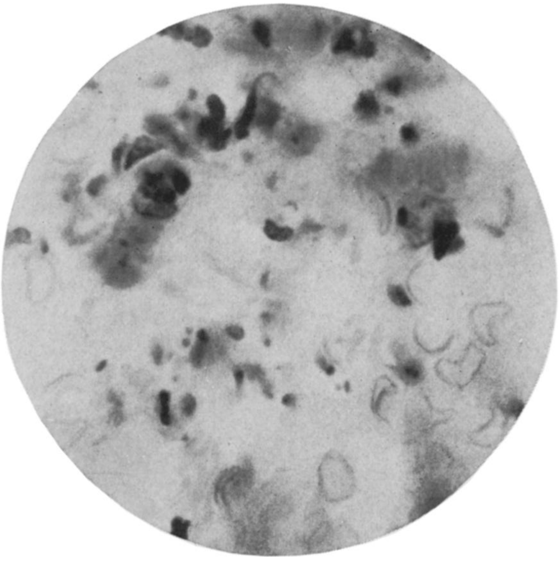

Figure 7.